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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/884,481	06/20/2001	Takao Hamakubo	P21128	9557

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EXAMINER	
FOLEY, SHANON A	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/884,481	HAMAKUBO ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 29 September 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☒ Applicant's reply has overcome the following rejection(s): 112, second.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See the correspondence attached*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: *none*.

   Claim(s) objected to: *none*.

   Claim(s) rejected: *1-8 and 15-28*.

   Claim(s) withdrawn from consideration: *none*.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Shanon Foley
Primary Examiner
Art Unit: 1648

Response to Request for Reconsideration

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 and 15-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grabherr et al. (Biotechniques. 1997; 22 (4): 730-735, cited previously), Possee (Current Opinion in Biotechnology. 1997; 8: 569-572, cited previously) and in further view of Nohturfft et al. (PNAS. 1999; 96: 11235-11240) and Duncan et al. (Journal of Biological Chemistry. 1997; 272 (19): 12778-12785) for reasons of record.

Applicant asserts that the rejection is improper because it does not clearly set forth how the documents are being combined. As an example of this assertion, applicant states that the rejection discusses general teachings of the references, but does not point to where it is taught or suggested in the documents for how the references are combined to arrive at the instant invention. Applicant requests that the Office clarify how the references are being combined and where the motivation is present in the combination of references to arrive at the instant method.

Applicant's assertions regarding the clarity of the rejection have been fully considered and are found unpersuasive. The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re*

Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). MPEP § 2144 specifically states:

> **The rationale to modify or combine the prior art does not have to be expressly stated in the prior art**; the rationale may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art, established scientific principles, or legal precedent established by prior case law (emphasis added).

Therefore, although the prior art is not required to expressly teach motivation, the motivations for expressing any protein of interest within a baculovirus are expressly found in the first full paragraph of the second column on page 570 of Possee et al. and the first full paragraph of the introduction section of Grabherr et al. These express teachings of Possee et al. and Grabherr et al. are specifically cited in the paragraph bridging pages 5-6 of the previous Office action.

The protein of interest is an ER protein and a Golgi Apparatus protein. More specifically, the protein of interest is SREPB-2. Duncan et al. study SREPB-2 and its expression in the ER and Norturfft et al. teach SREPB-2 expression in the Golgi Apparatus. Although neither reference teaches or suggests expression in a baculovirus system, one of ordinary skill in the art at the time the invention was made would have been motivated to express SREPB-2 in a baculovirus system to screen for ligands that may interact with SREPB-2 or further study the protein because baculovirus expression produces mammalian proteins in native conformation on the surface of the virus, see the first paragraph of the introduction section and the first paragraph of the first column on page 734 of Grabherr et al. and the first full paragraph of the second column on page 570 and the last paragraph on page 571 of Possee et al. These citations have previously been cited by the Office, see the paragraph bridging pages 4-5 of the non-final Office

action mailed December 2, 2003 and the last two paragraphs on pages 5-6 of the final rejection mailed June 29, 2004. Motivations for expressing SREPB-2 in a baculovirus system are expressly taught within the cited references and pointed out with direct citations in the final rejection. Therefore, there are no deficiencies within the final rejection. Applicant's assertions that the final rejection does not clearly set forth where motivation for combining the references is located within the references themselves is unfounded. Therefore, applicant's request for the withdrawal of finality of the previous Office action is denied.

Applicant summarizes the general teachings of each reference separately and concludes from this summary that "the combination of these documents teaches the expression of an intracellular organelle membrane-bound protein on the coat of a baculovirus if the protein has been fused to the major coat protein of a baculovirus." The examiner agrees that the combination of references teach expression of an intracellular organelle membrane-bound protein on the coat of a baculovirus if the protein has been fused to the major coat protein of a baculovirus.

However, applicant argues that the combined references do not teach or suggest recovering a budded baculovirus expressing an intracellular organelle membrane-bound protein.

Applicant's argument has been fully considered, but is found unpersuasive since Grabherr et al. separate, i.e. recover, a budded baculovirus virus expressing a recombinant protein on the surface of the virus from cell culture, see the second full paragraph on page 732 starting with the sentence beginning with "Concentrated virus particles..." to the last paragraph on page 735. Therefore, contrary to applicant's assertions, recovering a budded baculovirus expressing a recombinant protein on the surface of the virus, is expressly taught. The

combination of references clearly teach the expression of an intracellular organelle membrane-bound protein on the coat of a baculovirus and recovering the recombinant baculovirus to purify the recombinant protein expressed on the surface of the virus is expressly taught by Grabherr et al.

Applicant summarizes the general teachings of Duncan et al. and Nohturfft et al. and agues that neither reference teaches or suggests a method of recovering a budded baculovirus expressing an intracellular membrane-bound protein.

Applicant's arguments have been fully considered, but are found unpersuasive. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The combination of references teach all of the limitations recited in the claims. As discussed by applicant, Duncan et al. and Nohturfft et al. teach the specific protein of interest claimed, SREBP-2. As discussed above, motivation to express a protein of interest on the surface of a baculovirus is expressly taught by Grabherr et al. and Possee et al. The element of recovering a budded baculovirus that expresses a protein of interest on its surface is expressly taught by Grabherr et al.

Applicant states that the function of the recombinant protein fused to the major coat protein of a baculovirus of Grabherr et al. does not possess the same function as a non-fused protein. Applicant asserts that the instant protein is not fused to another protein and retains structural and functional properties.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., not fusing the

gene of a protein of interest to a baculovirus major coat protein) are not recited in the rejected claim(s). See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The claims do not require that the intracellular membrane-bound protein is un-fused. The instant claims require a baculovirus expressing an intracellular membrane-bound protein or a baculovirus containing a gene encoding an intracellular membrane-bound protein, which is what the combination of references teaches.

In conclusion, all of the limitations required by the claims are expressly taught by the references. Further, motivation to screen for ligands that may interact with SREPB-2 or further study SREPB-2 by expressing the protein in a baculovirus system and recovering the recombinant virus is expressly taught by the teachings of Possee et al. and Grabherr et al., see the previous citations above. In addition, the combination of references provides a reasonable expectation of success for expressing and recovering the SREPB-2 protein of Duncan et al. and Nohturfft et al. on the surface of the baculovirus of Grabherr et al. because Duncan teach studying SREPB-2 by forming a fusion protein and Grabherr et al. teach that expressing proteins on the surface of a baculovirus requires fusing a protein of interest to the baculovirus major coat protein, gp64. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to substitute the Ras portion of the fusion protein of Duncan et al. for the baculovirus gp64 protein of Grabherr et al. to express SREPB-2 on the surface of a baculovirus, since, according to Possee et al., any eukaryotic protein can be expressed and displayed on the surface of a baculovirus in light of the teachings of Grabherr et al. Therefore, all of the criteria for establishing a case of prima facie obviousness have been met and the rejection is maintained for reasons of record.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 10:00 AM - 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shanon Foley
Primary Examiner
Art Unit 1648